REMARKS

Claims 25 to 44 are pending in the application; claims 45 to 47 are withdrawn.

Claim Objections

Claim 41 is objected because it depends on itself; dependency has been corrected and claim 41 now properly depends from claim 40.

Rejection under 35 U.S.C. 102

Claims 25-39 and 42 stand rejected under 35 U.S.C. 102(b) as being anticipated by *Witwer et al. (US 6,174,670).*

Claim 25 has been amended to now set forth that the control nucleic acid is **added** in single-stranded form to the sample and furthermore that the detection is carried out at a temperature that is 2 degrees Celsius to 10 degrees Celsius below the melting temperature of the first product (features of claim 33).

In regard to the arguments presented before that the present invention provides a single-stranded control nucleic acid, Examiner has argued (on page 2 of the office action in response to the traversed restriction requirement; paragraph bridging pages 2 and 3 of the office action) that genomic DNA that is provided as a control nucleic acid is denatured during the initial PCR step so that a single-stranded form of nucleic acid is present.

The claim language has been clarified in that it is now stated that single-stranded nucleic acid is added to the sample, i.e., the control nucleic acid is from the start a single-stranded nucleic acid; no denaturation is required during PCR. The advantages of such a single-stranded control nucleic acid, especially an oligonucleotide, are explained in the specification (page 6, 2nd and 3rd paragraphs; paragraph bridging pages 6 and 7). *Wittwer et al.* nowhere discloses that a control nucleic acid should be added that is single-stranded. *Wittwer et al.* proposes only to employ gene fragments and the two gene fragments to be observed should be as similar as possible to one another.

According to the present invention, it is not at all required to employ a natural double-stranded fragment or a fragment that is very similar to the natural fragment. The inventor has found that single-stranded nucleic acids can be used as a control that, in contrast to the prior art assumption that close similarities in the regions of interest are required, a control nucleic acid can be used that deviates strongly from the nucleic acid to be detected. It is especially preferred that the control nucleic acids in a number of cases

are significantly shorter, i.e., they can be also deleted largely or even deleted with the exception of a few nucleotides (for example, 1 to approximately 10, up to approximately 20 or up to approximately 30). It is even possible in accordance with the present invention that the control nucleic acid comprises exclusively, or almost exclusively, the sequence regions that hybridize with the probes and the primers and cover them. This is explained in the instant specification in the paragraph bridging pages 6 and 7.

The step of adding a single-stranded control nucleic acid to the sample is therefore not anticipated by *Wittwer et al.* because *Wittwer et al.* only suggests double-stranded controls. The step of **adding a single-stranded control nucleic acid** to the sample is not disclosed or suggested.

The Examiner further argues that *Wittwer et al.* discloses testing of viral load in patients infected with HIV and hepatitis C by means of his method and that therefore single-stranded controls are inherently disclosed.

The only reference to HIV in *Wittwer et al.* is in connection with Example 19 where it is stated that:

"As a further example, quantification of viral load in patients infected with HIV or hepatitis C is important in prognosis and therapy. Using a control template and monitoring the efficiency of amplification of both control and natural templates during amplification, accurate quantification of initial template copy number is achieved."

There is no additional disclosure in regard to how to perform the test and there is no working example provided to demonstrate that the proposed application for HIV viral load is actually working. There is no suggestion as to the type of control to be used.

The simple statement that quantification of viral load is important in patients and that using a control during amplification can provide accurate quantification does not anticipate adding a single-stranded control nucleic acid to the sample absent any further teaching or disclosure as to the procedure, the compounds used, and the working conditions.

Moreover, there is no disclosure or suggestion in *Wittwer et al.* in regard to carrying out the detection at a temperature that is 2 °C to 10 °C below the melting temperature of the first product. The Examiner suggests that Fig. 48 in connection with col. 46, lines 42-46, shows that the detection is carried out at 2 °C to 10 °C below the melting temperature of the first product. The first product by definition (claim 25) is the product of the nucleic

acid to be detected and of the at least one single-stranded detection probe; the second product is the product of the added single-stranded control nucleic acid and of the at least one single-stranded detection probe. Example 23 deals with the detection of three genotypes - none of them is a control. There is therefore no first product to be detected and no second product providing a control. There is especially no teaching to carry out a detection at a temperature of 2 °C to 10 °C below the melting temperature of the first product. If homozygous mutant is considered the first product and a detection is carried out at 2 to 10 degrees Celsius below melting temperature (according to the diagram of Fig. 48 the melting point would be 66 degrees Celsius), the melting curve would stop between 56 and 64 degrees; this means that a differentiation between the products could not be made and that not even the homozygous mutant could be detected. The melting curve or detection in this range would be meaningless. Therefore, Fig. 48 and Example 23 cannot suggest the inventively proposed temperature range for detection.

Therefore, the instant claims as amended are not anticipated by or obvious in view of *Wittwer et al.*

Reconsideration and withdrawal of the rejection of the claims pursuant to 35 USC 102 are therefore respectfully requested.

Rejection under 35 U.S.C. 103

Claims 40, 41, 43, 44 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Wittwer et al.* and *Picard et al. (US 6,265,170).*

As discussed *supra*, the reference to *Wittwer et al.* cannot anticipate or make obvious the subject mater of claim 25; claims 40, 41, 43, 44 are believed to be allowable as dependent claims.

CONCLUSION

In view of the foregoing, it is submitted that this application is now in condition for allowance and such allowance is respectfully solicited.

Should the Examiner have any further objections or suggestions, the undersigned would appreciate a phone call or **e-mail** from the examiner to discuss appropriate amendments to place the application into condition for allowance.

Authorization is herewith given to charge any fees or any shortages in any fees required during prosecution of this application and not paid by other means to Patent and

Trademark Office deposit account 50-1199.

Respectfully submitted on June 27, 2007,

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